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Review article

# Microcirculation in anaesthesia: What every anaesthesiologist should know?

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ABSTRACT

Advances in knowledge have significantly enhanced our understanding of the structure and function of microcirculation. The tools used to study microcirculation have been refined and diversified. This review presents existing tools for anaesthesiologists and highlights two key areas where microcirculatory knowledge can be applied in anaesthesia: perioperative hemodynamic management and preoperative patient assessment. Preoperative microcirculatory assessment can identify dysfunction associated with chronic conditions and predict perioperative outcomes. This information allows for personalised patient management, improved counselling, and anticipation of postoperative complications. Intraoperatively, microcirculation monitoring provides valuable insights into tissue perfusion, guiding hemodynamic targets and fluid management. Despite its promising potential, integrating microcirculation monitoring into anaesthesia clinical practice presents challenges. Further research is needed to determine its prognostic value, refine monitoring tools, and validate the impact of microcirculation-focused interventions on patient outcomes.
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## 1. Introduction

Microcirculatory research has emerged as a rapidly evolving field, with a growing body of evidence underscoring its pivotal role in the development of organ dysfunction and multiorgan failure, directly impacting patient morbidity and mortality [1,2]. In the

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2352-5568/© 2025 The Authors. Published by Elsevier Masson SAS on behalf of Société Française d'Anesthésie et de Réanimation (SFAR). This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

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field of anaesthesia, as in intensive care medicine, hemodynamic management has traditionally focused on macrocirculation, with blood pressure and cardiac output serving as the primary indicators of hemodynamic status [3,4]. Although optimising cardiac output to ensure adequate tissue perfusion (in accordance with $VO_2$) and oxygen delivery constitutes a fundamental principle of hemodynamic management, this strategy often oversimplifies tissue perfusion by focusing solely on blood flow within major vessels [5]. Anaesthesiologists should consider the microcirculation, as this capillary network represents the ultimate site of oxygen, nutrient, and waste exchange between the blood and cells. Critically, macrocirculatory optimisation does not ensure adequate tissue perfusion in the presence of microcirculatory dysfunction. Advancements in tools and knowledge have enabled more detailed observations and understanding of microcirculation, allowing us to expand the focus of hemodynamic management to the relevant target of tissue perfusion, which plays a fundamental role in preserving organ function under conditions of physiological stress.

This narrative review aims to help anaesthesiologists understand new knowledge on the topic and the perspective for its application in perioperative medicine. We begin by summarising current knowledge of microcirculatory physiology and clearly defining key concepts, including hemodynamic coherence and tissue perfusion. Next, we introduce available techniques for assessing microcirculation and tissue perfusion, outlining their strengths, limitations, and potential clinical applicability. The following section discusses current evidence and potential applications of microcirculatory monitoring in perioperative medicine, specifically focusing on preoperative patient assessment and intraoperative hemodynamic management. Finally, we provide practical suggestions and propose clinical pathways for integrating microcirculation assessment into anaesthetic practice, aiming ultimately to improve patient outcomes.

## 2. Definition and functions of microcirculation

The microcirculation refers to the intricate network of arterioles, capillaries, and venules smaller than 200 microns, functioning collectively as a distributed dynamic 'microorgan,' embedded within tissues [6]. The capillary bed constitutes its functional unit, orchestrating the vital exchange of oxygen, nutrients, metabolic products, and signalling molecules between blood and parenchymal cells. Endothelial cells line the inner surface of capillaries and represent over 90% of the body's total endothelial surface, and play an important role in many vital functions (Fig. 1). This endothelium, covering about 5000 $m^2$, actively maintains tissue perfusion, defined as the delivery of blood flow, oxygen, and nutrients to tissues at the cellular level through dynamic adjustments in vascular tone and capillary density, thereby maintaining homeostasis and supporting organ function [1,7]. Tissue perfusion itself depends on the balance between convective forces (driven by cardiac output and intravascular pressure gradients within the microvasculature, from inflow to outflow) and diffusive forces (determined by capillary density, distance from capillaries to target cells). Covering the endothelium is the glycocalyx, a protective surface layer with a thickness ranging from 0.2 to 2 μm composed of proteoglycans, glycosaminoglycans, and plasma proteins [8]. This structure regulates vascular permeability and coagulation [2]. Glycocalyx shedding, commonly seen during major surgeries, increases vascular permeability, exposes various adhesion molecules and tissue factor, the initiator of the coagulation cascade, which then has a procoagulant function [9,10]. Damage to this barrier is associated with microvascular dysfunction, and contributes to tissue oedema and plays a pivotal role in the pathophysiology of organ failure, particularly under stress conditions such as shock or surgical trauma [11–15].

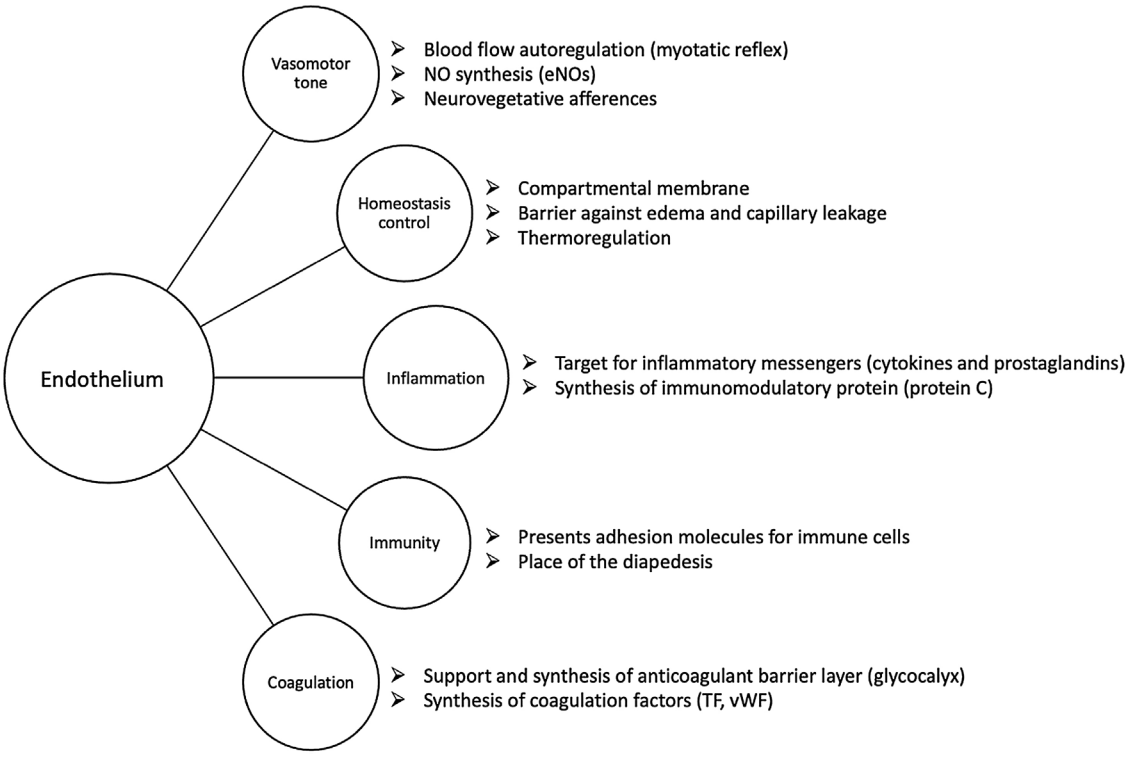



**Fig. 1.** Endothelium at the centre of vital function assumed by the microcirculation.
NO: Nitrite oxide. eNOs: endothelial NO synthase. TF: Tissue factor. vWF: von Willebrand factor.

*Understanding hemodynamic coherence*

Hemodynamic coherence refers to the condition where resuscitation efforts that improve systemic hemodynamic variables (macrocirculation) also effectively correct regional and microcirculatory perfusion, ensuring adequate oxygen delivery to parenchymal cells (Fig. 2) [16]. This allows cells to maintain their functional activities and support organ function. Under physiological conditions, macrocirculation and microcirculation operate in a 'coupled' state, maintaining this coherence. However, in pathological states characterised by significant systemic inflammation, this coherent link can be disrupted [2,17]. This loss of hemodynamic coherence signifies a state where conventional hemodynamic management fails to adequately restore microcirculatory perfusion and oxygen delivery to parenchymal cells; organ dysfunction may persist or worsen despite resuscitation efforts.

Some studies in the literature have described conditions of intraoperative loss of hemodynamic coherence, in which resuscitation performed by the anaesthesiologist resulted in divergent responses between systemic hemodynamic variables that did not lead to a parallel improvement in microcirculatory tissue perfusion and oxygenation [18–20]. Like sepsis, nonseptic conditions, including pancreatitis, ischemia-reperfusion, burns, and surgical trauma mediated by damage-associated molecular patterns (DAMPs), can elicit significant systemic inflammation and result in a loss of hemodynamic coherence, an impairment that is particularly frequent in cardiac surgery involving cardiopulmonary bypass (CPB) [21]. This understanding illuminates why maintaining macrocirculatory stability during surgery is insufficient to guarantee adequate tissue perfusion and subsequent organ protection. The concept of loss of coherence may explain the negative results of several studies of intraoperative hemodynamic targeting therapy aimed at normalising or even supranormalising systemic oxygen delivery variables [22–26]. In a situation of loss of hemodynamic coherence, which is likely, normalisation of the systemic circulation without a parallel improvement in the microcirculation would indeed have been futile. Guidelines' recommendation against routinely maximising stroke volume or cardiac output, and instead advocating for individualised targets based on signs of tissue perfusion and oxygenation, underscores the critical importance of intraoperative monitoring that goes beyond macrohemodynamics to assess tissue-level perfusion [4]. Therefore, it is important to identify indicators that can be used to monitor tissue perfusion, particularly in intensive care patients requiring surgery, especially those with septic shock, who are at high risk of loss of coherence [27].

## 3. Clinical assessment tools for microcirculation

The study of microcirculation is difficult because of the size of the vessels studied and the subtle reactivity of the microvasculature. In this section, we describe the different methods used to study microcirculation. Among the many functions of microcirculation, our focus here is on its primary role: perfusion of the capillary bed and its regulation by vasomotricity. Tissue perfusion is the result of the combined performance of macro- and microcirculation. In this interdependent system, hemodynamic failure can lead to alterations in microcirculatory parameters. However, microcirculatory changes are not always the result of macrocirculatory failure; microcirculation may exhibit abnormalities that lead to tissue hypoperfusion and therefore warrant specific monitoring.

### 3.1. Clinical examination

Clinical examination offers valuable insights into tissue perfusion, providing a readily accessible and repeatable method for bedside assessment (Table 1). Skin perfusion has demonstrated a good correlation with the perfusion of intra-abdominal organs and has also been related to relevant clinical outcomes [28,29]. The appearance of mottling provides the clinician with sensitive

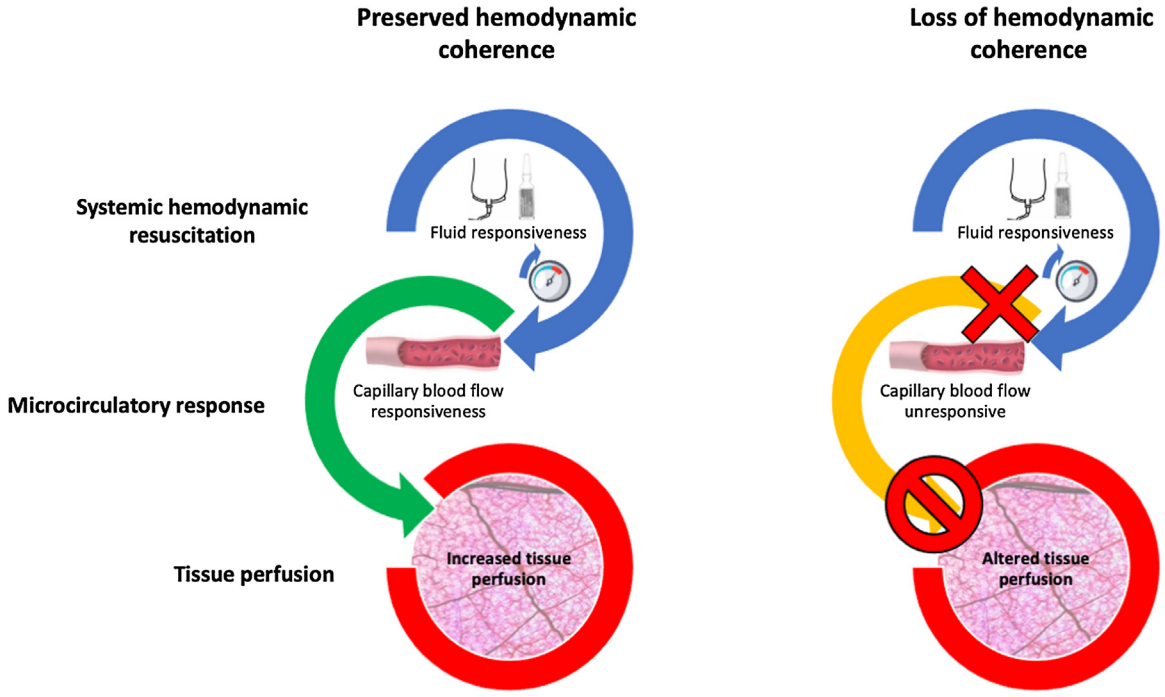



**Fig. 2.** Hemodynamic coherence between macrocirculation and microcirculation.
This figure illustrates the concept of hemodynamic coherence, where improvements in macrocirculatory parameters (blood pressure, cardiac output) are accompanied by improvement in microcirculatory perfusion. Loss of coherence refers to situations in which hemodynamic optimisation fails to restore adequate microcirculation and tissue perfusion.

**Table 1**
Noninvasive techniques used for microcirculatory measurement, intraoperatively or immediately postoperatively.

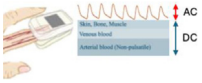
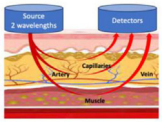
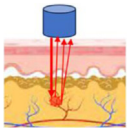
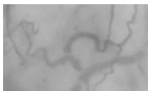
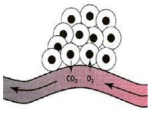
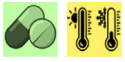
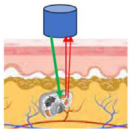
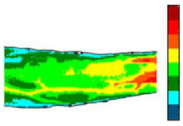
| Techniques | Description | Advantages | Limits | Possible tests |
|---|---|---|---|---|
| Clinical exam<br>– Capillary refill time (CRT)<br>– Mottling | Macroscopic study of tissue perfusion by observation (mottling) or compression / release of the skin (CRT). | No device required, free,<br>Repeatable as necessary. | Intermittent measurement,<br>Inter-operator variation,<br>Variation between locations (CRT) & between skin colors (mottling).<br>Variable intraoperative accessibility | |
| Perfusion index = AC/DC<br>  | Photoplethysmographic method evaluating the pulsatile and non-pulsatile parts of the signal.<br>Measurable peripherally (digital) or centrally (urethral) | Common device without consumables,<br>Continuous monitoring. | Need for sufficient signal quality (peripheric),<br>Complex analysis (many determinants),<br>Variation between locations & limbs positions. | |
| Tissular near infrared spectroscopy (NIRS)<br>  | Measurement of tissue oxygenation by differential absorption by haemoglobin contained in the tissue volume under the sensor.<br>2Dimensions: hyperspectral imaging | Not accurate (+/- 1%),<br>Continuous monitoring. | Absorption of arterial, capillary and venous blood mixture.<br>Local variability (except 2D),<br>Variation between locations. | |
| Laser-Doppler<br>  | Fluxmetry of red blood cells in the target volume explored by a laser using the Doppler effect.<br>Standard: 1 measuring point,<br>2Dimensions: laser Speckle imaging. | Accuracy,<br>Continuous monitoring. | Application in research,<br>Relative unit of measurement,<br>Local variability (except 2D). | |
| Sublingual videomicroscopy<br>  | Optical imaging of microvascular content.<br>Videomicroscopy enables visualisation of the sublingual microcirculation and quantified the flow of red blood cells and the density of the capillary (structural & functional analysis). | Only method for structural study of the microcirculatory,<br>Repeatable as necessary,<br>(Semi)automatized analysis available. | Application in research,<br>Numerous artefacts,<br>Requires training, Time consuming. | |
| Tissular carbon dioxide partial pressure ($TpCO_2$)<br>  | Tissular $CO_2$ pressure depends on the balance between cellular production and elimination by capillary blood flow. Possibility of calculating the tissue-to-arterial $CO_2$ pressure gradient.<br>Numerous measurement sites: Cutaneous or organ (stomach, bladder). | Continuous monitoring. | Application in research,<br>Variation between locations. |  |
| Mitochondrial oxygen tension<br>  | Topical 5-aminolevulinc acid administration enhances mitochondrial protoporphyrin IX levels and the principle of delayed fluorescence detection after an excitation pulse with green (510 nm) light. Emission light is the delayed fluorescence (red light, 630–700 nm) and its lifetime is oxygen-dependent. This technique enables quantification of cutaneous mitochondrial oxygen tension and consumption, reflecting the balance between oxygen supply and demand at the cellular level where oxygen is ultimately utilised. | Only method for estimate the mithocondrial energetic balance.<br>Continuous monitoring. | Application in research,<br>Topical application of 5-aminolevulinic acid for at least 5 h is required to achieve adequate protoporphyrin IX concentrations for measurement,<br>Unknown variation between locations. | Unknow |

**Table 1** (*Continued*)

| Techniques | Description | Advantages | Limits | Possible tests |
|---|---|---|---|---|
| Skin temperature | Assessment of peripheral perfusion via the thermal conduction of blood flow. It can be evaluated at a single point, or as a temperature gradient between proximal and distal sites (*e.g.*, forearm-to-fingertip) or between central and peripheral regions. | Common device, | Complex analysis (many determinants), | |
| | Standard: 1 or 2 measuring point, | Very user friendly, | Need to be isolated from the ambient atmosphere, | |
| | 2Dimensions: thermographic camera. | Continuous monitoring. | Variation between locations & positions. | |
|  | | | | |

AC: alternating current,
DC: direct current.

information about the patient's tissue perfusion. Limitations of mottling assessment include the difficulty of evaluating mottling in patients with dark skin or when the knees are not visible (due to surgical fields). Similarly, the capillary refill time (CRT), which measures the speed of skin recolouration after being blanched by manual pressure, remains a very simple means of repeated bedside assessment. In a prospective study of 111 postoperative patients who underwent major abdominal surgery, alterations in peripheral perfusion (defined as CRT $>$ 4.5 s and/or perfusion index $<$ 1.4 and/or forearm-to-fingertip temperature gradient $>$ 2 °C) were associated with the development of severe complications, independent of systemic hemodynamics [30]. While finger CRT is standard, arm elevation significantly alters values; earlobe CRT may offer a viable alternative when finger access is limited, but further clinical studies are needed to validate site-specific CRT interpretation in diverse surgical scenarios [31].

### 3.2. Biological variables

Repeated arterial lactate measurements have been proposed to assess anaerobic metabolism and the mismatch between perfusion and tissue oxygen needs. However, this method has limitations. It cannot be used for immediate monitoring because it requires regular sampling, reflects only the balance between lactate production and elimination and allows for delayed monitoring. In specific surgical contexts such as liver and kidney surgeries, lactate interpretation may be further confounded by impaired clearance and altered metabolism, which can affect lactate kinetics independently of tissue perfusion. Moreover, anaerobic metabolism is only one of the potential sources of blood lactate production, and the anaerobic origin of lactate is debated. Aerobic glycolysis, particularly in stress situations, is a significant pathway for lactate generation that is independent of tissue hypoperfusion [32,33]. Under these conditions, an increase in lactate levels between two measurements during resuscitation is not pathognomonic of the inefficiency of the hemodynamic therapies initiated, and the Surviving Sepsis Campaign clearly states that lactatemia cannot be used as a measure of tissue perfusion [34]. The high prognostic value of lactate levels in critically ill patients may be related to stress mechanisms, dysoxia and inflammation [33,35].

### 3.3. Monitoring tools

#### 3.3.1. Global indicators

Tissue perfusion can be assessed via global indicators that reflect the integrated functions of macrocirculation, microcirculation, and cellular oxygen utilisation (*e.g.*, $PCO_2$ gap and venous oxygen saturation ($SvO_2$)) (Table 1). SvO? has been used to evaluate the balance between oxygen delivery and consumption and is correlated with cardiac output and the veno-arterial CO? gradient. However, its role as a therapeutic target remains limited due to inconsistent effects on mortality and uncertain normal values [36]. Low SvO? levels may reflect increased tissue oxygen extraction, which can occur either in response to heightened metabolic demand or as a consequence of reduced tissue perfusion. Conversely, elevated SvO?, often resulting from microcirculatory shunting or mitochondrial dysfunction, has been linked to increased mortality, particularly in septic shock [37,38]. This underscores that while SvO? can be influenced by microcirculation and tissue perfusion, it does not reliably reflect local tissue perfusion and should not be used in isolation to guide therapy [39].

#### 3.3.2. Sublingual videomicroscopy

Sublingual videomicroscopy (Table 1) is the most advanced tool in anaesthesia and intensive care for the local study of microcirculation. The use of sublingual videomicroscopy in anaesthesia has been extensively described by Flick *et al.* [40]. Briefly, handheld vital videomicroscopy is a portable intravital videomicroscopy technique for direct visualisation of the sublingual capillary bed. This technique provides detailed structural and functional analysis, yielding critical insights into determinants of tissue diffusion, such as capillary density, capillary haematocrit, and erythrocyte distribution within capillaries (reflecting the distance between the red blood cell or capillary and the cell). Assessment of tissue perfusion focuses on microcirculatory function using validated metrics of convective and diffusive forces such as the microvascular flow index (MFI), total vessel density (TVD), and proportion of perfused vessels (PPV) [41]. The perfused boundary region (PBR) (Table 2), which serves as an indicator of glycocalyx integrity, is the peripheral band formed by rheological forces that cause red blood cells to circulate in the centre of the capillary [42].

Interestingly, characteristic microvascular sublingual abnormalities persisting despite macrocirculation optimisation after systemic injury, including heterogeneity of perfusion manifested as adjacent regions of well-perfused and non-perfused capillaries, arteriovenous shunting characterised by the coexistence of poorly perfused areas and regions where red blood cells move at high velocities, leukocyte activation or rolling, reduction in glycocalyx thickness, and tissue oedema increasing oxygen diffusion distances [1,41,43–46]. Despite significant technological improvements, including automated analysis software, widespread adoption in clinical practice remains limited due to ongoing challenges, notably difficulties in consistently obtaining high-quality images, variability between study sites, and the time-consuming nature of manual analysis [47–49].

**Table 2**
Tests coupled with measurement techniques for intraoperative or immediate postoperative microcirculatory assessment.

| Tests | | Description | Advantages | Limits |
|---|---|---|---|---|
| | Measurements before/after systemic hemodynamic action or therapy | Increase/decrease cardiac output (fluid challenge, vasopressor, inotrope), vasodilator (ilomedine), blood transfusion, . . . | Direct analysis of therapy effect,<br>Noninvasive | Requires a rapid microcirculation response. |
| | Vaso-occlusion test | A limb placed in ischemia for a short period (3−15 min) usually by placing a cuff. PORH is observed during the reperfusion phase.<br>Sensory nerves are a major contributor to PORH. Results are conflicting concerning the implication of prostaglandins and NO pathway. | Simple, available, noninvasive. | Occlusion >3 min is uncomfortable for patient.<br><br>PORH is not specific to any one mechanism or pathway. |
| | Thermal challenge | A temperature of 42–44 °C is applied on the skin and induced a biphasic response without being painful.<br><br>The first peak (2−3 min) is dependent on the autonomic nervous response, followed by a later plateau (20−30 min) dependent on the NO pathway. | Clearly identified signalling pathways. | Test time-consuming & requires special equipment,<br>Temperature must be kept constant,<br>Local cooling is less studied. |
| | Local administration of pharmacological agent | Infusion of vasoactive molecules enables a specific microcirculatory response to be observed. The technique must not provoke a vascular local reaction.<br>Iontophoresis works like electrophoresis on the skin, enabling the non-invasive transfer of electrically charged molecules (acetylcholine or SNP) | Signaling pathway specific, | Requires special equipment,<br><br>Iontophoresis induces also current-induced vasodilation (CIV), |
| | | Micro-dialysis, micro-injection. | Highly relevant for research. | Local temperature should be kept constant,<br>Invasive & topical anaesthesia significantly mitigates the response (micro-dialysis, injection). |
| | Measuring thickness of the glycocalyx layer | The perfused boundary region (PBR), based on the principle that red blood cells flow deviate from the centre when the glycocalyx is impaired, can be analyzed as an indicator of glycocalyx integrity. | Only method for structural glycocalyx study. | Requires special equipment and good quality videomicroscopy recording,<br>Same limitations as videomicroscopy,<br>Application in research. |

PORH: post occlusive reactive hyperemia, NO: nitrite oxide, SNP: sodium nitroprusside.

### 3.3.3. *Methods based on tissue light absorbance*

Tissue light absorption varies with haemoglobin content, oxygen saturation, and mitochondrial metabolism, enabling techniques such as near-infrared spectroscopy (StO?), mitochondrial oxygen tension and the perfusion index (PI), which is the ratio of pulsatile to non-pulsatile photoplethysmography (PPG) signals, to assess local microcirculatory function and tissue perfusion through red blood cell flow (Table 1). PPG is a non-invasive, cheap, rapid, and simple-to-use technology, but interpreting PPG data can be challenging. The principle of conventional PPG is based on the measurement of tissue volume variations through changes in light absorption. Light absorption fluctuates during the cardiac cycle, reaching its maximum in systole when vessel dilatation under arterial pressure increases local blood volume beneath the light source. The photodetector captures this signal, which is decomposed into a pulsatile component, the "alternating current" (AC), and a non-pulsatile component, the "direct current" (DC). AC represents changes in light absorbance caused by pulsatile vessels. Importantly, AC is not a direct measure of blood flow but rather an indicator of volume changes. DC reflects light absorption from capillaries, venous vessels, skin, soft tissue, and bone. The perfusion index (PI) is calculated as the ratio of AC/DC, representing the relative contribution of pulsatile arterial blood flow to overall tissue absorbance. When measured at a peripheral site, PI reflects both systemic and local factors. Locally, it is influenced primarily by vascular tone, while centrally it depends on stroke volume. For example, in moderate vasoplegia, reduced vascular tone causes arterial vasodilation without significant changes in stroke volume, resulting in an increased PI. In severe vasoplegia, concurrent arterial and venous vasodilation reduces stressed volume and venous return, leading to a secondary drop in stroke volume and, consequently, a decrease in PI. Conversely, in hypovolaemia or cardiogenic shock, reduced stroke volume combined with increased peripheral vasoconstriction contributes to a decrease in PI.

The measurement of the PI appears promising as a quantified, continuous indicator of tissue perfusion [50]. In a retrospective study of 1338 high-risk surgical patients, an intraoperative PI $\leq$ 0.5 or 1.5 was associated with an increased incidence of severe postoperative complications and mortality (OR 1.79, 95% CI 1.02–1.09; p = 0.02 and OR 1.65, 95% CI 1.20–2.27; P = 0.002, respectively) [51]. In a previously cited study, a PI $<$ 1.4 was one of the indicators of low tissue perfusion associated with postoperative complications in major abdominal surgery [30]. However, uncertainty remains regarding the kinetics of onset and correction during hemodynamic changes.

Similar to conventional peripheral PPG, urethral-PPG represents an innovative approach for central microcirculatory assessment. Using a small infrared probe integrated into a Foley catheter, urethral PI measures changes in mucosal blood volume and flow, providing continuous, minimally invasive hemodynamic monitoring of a central organ. Urethral PI has been successfully employed in clinical settings such as off-pump coronary artery bypass surgery and liver surgery [52,53]. It demonstrated potential for monitoring goal-directed therapy and identifying situations of impaired hemodynamic coherence [53,54].

Emerging data also suggest the value of mitochondrial oxygen tension as an early indicator of tissue hypoxia (Table 1). Mitochondrial oxygen tension is based on delayed fluorescence of protoporphyrin IX using the triplet state lifetime technique after upregulation by a self-adhesive patch containing 5-aminolevulinc acid at least 5 h before measurements. In two pilot studies, a low mitochondrial oxygen tension (<30 mmHg) at ICU admission and the duration spent below this threshold predicted acute kidney injury in cardiac surgery patients earlier than elevations in lactate levels [59,60].

#### 3.3.4. Other local indicators

Additional techniques have been developed to assess local microcirculatory function and tissue perfusion. The tissue perfusion can be measured by the red blood cell flow through a capillary bed across a volume of tissue by laser Doppler, tissue CO? partial pressure, reflecting the balance between cellular CO? production and elimination via capillary blood flow, and the skin temperature gradient between proximal and distal sites, reflecting the thermal conduction via capillary blood flow (Table 1). Mismatches between perfusion and local metabolic demand are associated with a wide range of acute conditions, from organ failure to myocardial ischemia and wound-healing difficulties [43]. For example, skin temperature, especially forearm-to-fingertip temperature gradient, strongly correlated with skin blood flow measured by laser-Doppler ($r$ = 0.828), and gradient $>$ 2 °C was associated with the development of complications in major abdominal surgery [30,55].

Tissue $CO_2$ (or the tissue-to-arterial $pCO_2$ difference) is a candidate for assessing local perfusion deficit. This method, using non-invasive, continuous cutaneous sensors, has shown promise in providing a rapid and dynamic assessment of peripheral microcirculatory perfusion, notably in septic shock [56–58].

Recognising that microcirculatory alterations can be heterogeneous across a single point or a small volume of tissue, newer imaging tools such as the laser Speckle imager and hyperspectral imager enable a much larger 2-dimensional exploration. While these tools offer the advantage of assessing broader regions, their reliance on complex post-processing currently limits their feasibility for routine bedside application. Ultimately, local indicators offer insight into microcirculatory function at the measurement site, which may not reflect perfusion in other organs, and should therefore be interpreted in conjunction with systemic parameters and clinical context.

### 3.4. Measuring microcirculatory vasoreactivity

Depending on the clinical situation, at baseline, in a resting or healthy organism, it may be difficult to obtain useful information from a static measurement of tissue perfusion, regardless of the method used. There are two explanations for this: (i) microcirculation may appear normal at rest but be in a state of compensation for insufficiency, and (ii) most of the methods described do not have defined normal values. In this context, relative measurements are used, with the basal value used as the reference. The purpose of these dynamic tests is to expose microcirculation to a calibrated local stimulus and measure the microcirculatory response and functional vascular recruitment (Table 2). Such tests can be performed in a stable clinical (or basal) state that appears functional to unmask a pathological microcirculatory response and in a pathological context to explore the impairment of the ability of the microcirculation to adapt functionally.

Vasomotricity is therefore the main response of the circulatory system, and Poiseuille's law helps in understanding the importance of arteriolar vasomotricity in controlling blood flow distribution. Poiseuille's law states that flow is directly proportional to the pressure difference along a vessel ($\Delta P$), to the power of 4 of its radius (R), and inversely proportional to its length (L) and the viscosity of the fluid ($\mu$).

$$Flow = \frac{\Delta P \pi R^4}{8 \mu l}$$

As a result, the arteriolar diameter is an important parameter of regional blood flow, and small changes in diameter can significantly alter vascular resistance to blood flow in the vessel. The study of vasoreactivity involves tests in which a biochemical (acetylcholine, nitroprusside) or physical (heat, ischemia) stimulus is used to induce a vascular response, often vasodilation, to replicate the adaptation necessary for increasing tissue metabolism. The effect of this stimulus on tissue perfusion is recorded by one of the functional testing methods described above. Various perfusion indicators can be used to measure the response to vasoreactivity tests, providing information on the adaptive capacity of the microcirculation.

The simplest and most accessible test is the vaso–occlusive test [61,62], in which a limb is subjected to ischemia for a short period (3–5 min) (Table 2). Reperfusion is accompanied by postocclusive reactive hyperaemia (PORH), which is mainly endothelium-dependent and can be measured by tissue NIRS or by changes in the pulsatility signal index. As measured by vascular echo Doppler, the vasodilation observed in arteries upstream and downstream of the ischemic zone is called flow-mediated vasodilation (FMV).

Another test involves the local application of a heat source. Local thermal cutaneous hyperaemia to heat has been well described [63] and typically involves a biphasic vasodilatory response in laser Doppler (Table 2). The initial peak is dependent on the autonomic nervous response, followed by a later plateau dependent on the endothelium via the nitric oxide (NO) pathway [61].

Local injection of vasoactive molecules is not possible because the injection provokes a local vascular reaction. Microdialysis and iontophoresis (electrophoresis on the skin surface) allow minimal or noninvasive infusion of the molecules of interest (Table 2) [61]. The local application of vasoactive molecules has also been described. Sublingual videomicroscopy allows the measurement of recruited and nonrecruited capillary vessel density in response to an endothelium-dependent (acetylcholine) or endothelium-independent (nitroprusside) vasodilator [64,65]. These methods require specialised equipment that is currently only available for research purposes. These dynamic assessments of microcirculatory recruitment are at the origin of the concept of physiological microcirculatory reserve. This functional reserve corresponds to the perfusion gain obtained by optimising the microcirculatory flow (convective reserve) and capillary density (diffusive reserve) during dynamic testing [65,66].

## 4. Application of microcirculatory assessment in anaesthesiology

### 4.1. Preoperative basal microcirculation as a prognostic marker prior to surgery

Anaesthesia is a unique situation in medicine, where a physician can sedate a physiologically healthy patient. In elective surgery, prior to the induction of anaesthesia, the patient is in a stable clinical state, where, in most cases, the cardiovascular system provides tissue perfusion adapted to the patient's metabolic needs. Anaesthesia and surgery represent acute critical episodes that challenge a patient's tissue perfusion. This situation presents specific opportunities for using microcirculatory assessment to refine a patient's perioperative risk preoperatively.

Several studies highlight the potential of preoperative microcirculatory assessment in predicting postoperative outcomes. In coronary artery bypass grafting (CABG) patients, Feng *et al.* found that poorly controlled diabetes impaired arteriolar function both before and after CPB, with reduced vasodilatory responses [67]. In a separate study using sublingual videomicroscopy in 35 patients undergoing major abdominal surgery, a lower preoperative MFI was associated with postoperative complications [68]. In a series of articles, Gokce *et al.* demonstrated that impaired FMV before vascular surgery predicted short- and long-term major adverse cardiovascular events, while nitroglycerin-induced vasodilation remained unchanged [69–71]. Similarly, in 218 noncardiac surgery patients with intermediate or high cardiovascular risk, preoperative endothelial dysfunction assessed via peripheral arterial tonometry (EndoPAT-2000, Itamar Medical, Atlanta, USA) was linked to postoperative myocardial injury, though not to acute renal failure [72,73]. These methods of PORH measurement (Doppler and tonometry) have not been widely developed, and equipment is not available at most centres. In another prospective cohort of 60 planned cardiac surgery patients, skin capillary vasodilation induced by acetylcholine (endothelium-dependent vasodilation) was measured via laser Speckle. Patients with postoperative organ dysfunction (defined by a sequential organ failure assessment (SOFA) score $> 3$ at 48 h) presented a delayed peak of vasodilation in response to acetylcholine compared with patients without postoperative organ dysfunction (133 s [104–156] *vs.* 98 s [76–139], $P = 0.016$) [74]. The time to peak and amplitude of endothelium dependence and vasodilation were independently associated with the occurrence of organ dysfunction and acute kidney injury in multivariate models adjusted for other risk factors for postoperative complications [74,75].

Studies have demonstrated that preoperative evaluation of microcirculatory functional reserve is feasible and may be valuable, with certain parameters linked to patient outcomes [69–72,74]. Assessing vascular bed reactivity before surgery may help identify patients at risk of microcirculatory failure under surgical stress and serve as a prognostic marker [76]. This offers a unique opportunity to anticipate and personalise perioperative care. Such data could inform therapeutic decisions, patient management, and the consent process [77]. A conceptual integration of these parameters into preoperative and intraoperative care is illustrated in Fig. 3. However, a causal relationship between microcirculatory dysfunction and perioperative complications remains unestablished. Altered microcirculatory reactivity has been observed in chronic conditions like diabetes, hypertension, renal failure, and ageing, raising the possibility that it may reflect underlying risk factors [78–80].

**Suggestion n°1:** Pending validation of tools for measuring microcirculatory functional reserve, it is important to keep in mind the risk of microcirculatory failure in patients likely to have chronic impairment of microcirculation (diabetes, hypertension, chronic renal failure, and advanced age).

### 4.2. Improving and protecting the tissue perfusion

Navigating the literature on microcirculation presents a considerable challenge for anaesthesiologists, due to the large volume of evidence derived from the ICU. Although seemingly distinct, the operating theatre and ICU share common patient profiles, facilitating a degree of translation between settings. Critically ill patients with organ failure and shock, whether of hypovolaemic, cardiogenic, or vasoplegic origin, are encountered frequently in both environments, suggesting potential applicability of findings across these clinical contexts. Conversely, fewer critically ill patients without organ dysfunction are primarily managed in perioperative settings. Studies show that hemodynamic coherence is predominantly preserved in these patients [81]. Importantly, major surgery and anaesthesia themselves represent substantial physiological stressors capable of inducing organ dysfunction through mechanisms such as vasoplegia, haemorrhage, and inflammation. Microcirculation has been recognised as a prognostic marker in anaesthesia, but it remains unclear whether it is merely a marker or an actual risk factor. Determining whether perioperative complications can be directly attributed to microcirculatory dysfunction is essential. If causality is established, it opens the possibility for targeted interventions aimed at protecting or improving microcirculatory function from the preoperative period onward, potentially reducing perioperative complications. Nevertheless, the operative environment introduces unique constraints on microcirculatory assessment (*e.g.*, limited access due to drapes and surgical fields), which differ notably from ICU conditions.

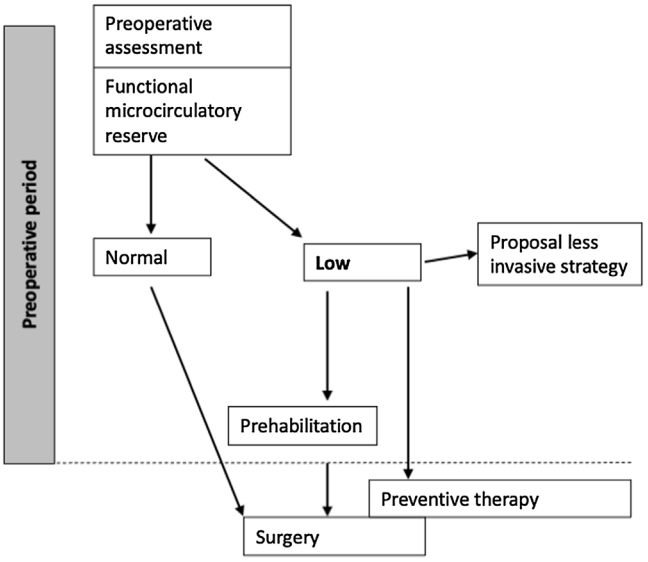



**Fig. 3.** Suggested preoperative course taking into account preoperative microcirculatory assessment.
This is a proposed preoperative pathway that incorporates microcirculatory assessment, such as assessment of functional microcirculatory reserve, to identify patients at risk of perioperative complications. Based on the results, strategies may include prehabilitation before surgery, preventive measures such as advanced intraoperative microcirculatory monitoring, or the consideration of less invasive surgical approaches. This approach supports personalised risk stratification, perioperative optimisation, and informed shared decision-making.

#### 4.2.1. Targeting a preoperative improvement in microcirculation

One promising direction is the development of preventive strategies that optimise microcirculation in patients with abnormal preoperative microcirculatory parameters. For example, in a small study of 10 heart failure patients, a 12-week rehabilitation program led to improved microcirculatory reactivity [82]. Thus, prehabilitation programs might consider enhancing microcirculatory function as a target (see Fig. 3).

#### 4.2.2. All-in on macrocirculation? Rethinking intraoperative hemodynamic targets

Cardiac output monitoring tools have become more user-friendly and widely available, as well as cardiac output measurement has taken centre stage in managing patient hemodynamics. Current guidelines recommend goal-directed therapy (GDT) where the administration of fluids and catecholamines is conducted to normalise systemic hemodynamic parameters such as cardiac output and blood pressure [4,83]. While a meta-analysis including 76 randomised controlled trials and 9081 patients suggested that

GDT can reduce certain postoperative complications, this approach has limitations [84]. Defining the optimal cardiac output for individual patients is challenging, and the focus on macrocirculation may not guarantee adequate tissue perfusion and oxygenation – the true target of hemodynamic management [16]. Indeed, GDT can lead to "overoptimization" and iatrogenic effects such as tissue hypoperfusion, fluid overload, and glycocalyx degradation [15,85–87]. Even when systemic hemodynamics are optimised, microcirculatory alterations may persist, contributing to perfusion impairments, organ dysfunction, and increased mortality [11,88,89]. This disconnect highlights the need for more direct intraoperative assessment of tissue perfusion. Recent clinical studies have demonstrated the feasibility and safety of integrating microcirculatory assessment into GDT during major abdominal surgery. The CUSTOM trial showed that both stroke volume maximisation and maintenance of preoperative cardiac index increased perioperative oxygen delivery compared to routine care, suggesting that hemodynamic coherence was maintained [90]. Similarly, a randomised trial using an Assisted Fluid Management system to guide fluid therapy reported significantly improved sublingual microvascular flow, higher stroke volume and cardiac index, and lower lactate levels compared to standard GDT [91]. These findings support the potential complementarity of GDT and microcirculatory monitoring, reinforcing that optimisation through structured protocols can be achieved without compromising, and possibly enhancing tissue perfusion.

Several studies have investigated the intraoperative microcirculation, but isolating the specific effects of anaesthesia *versus* surgery is challenging. Changes in microcirculation can be observed intraoperatively, more frequently in cardiac surgery than in non-cardiac surgery. A review of the literature is provided in the Appendix B. Existing evidence suggests that anaesthesia-induced compensatory mechanisms may initially reduce the capillary bed to maintain systemic hemodynamics [81,92]. Hemodynamic coherence between macro- and microcirculation is generally preserved until these mechanisms are overwhelmed, leading to vasoplegia, capillary recruitment, and loss of coherence. Furthermore, studies suggest potential intraoperative decreases in vasoreactivity; this highlights the potential inadequacy of blood pressure or cardiac output targets as surrogates for tissue perfusion, which assume consistent hemodynamic coherence [93,94]. Flick *et al.* showed an association between intraoperative PPV alteration (<92%) and postoperative complications [89]. Currently, no validated method exists for monitoring this coherence. Nonetheless, studies in the field of intensive care suggest that microcirculation-directed interventions, such as those targeting CRT, can decrease the need for vasopressors, reduce organ failure and improve outcomes, sometimes independent of changes in systemic hemodynamics [95–97]. These findings, along with the observation that improvements in microcirculatory indicators such as mottling score and CRT often correlate, strongly indicate the potential of microcirculatory monitoring to personalise and optimise intraoperative hemodynamic management.

**Suggestion n°2:** Clinicians should be aware that solely optimising macrocirculation (cardiac output, blood pressure) may not guarantee adequate tissue perfusion, as microcirculatory alterations can persist despite seemingly normal systemic hemodynamics; therefore, microcirculatory monitoring should be considered to better personalise intraoperative hemodynamic management and potentially improve patient outcomes.

#### 4.2.3. Paving the way for intraoperative volume expansion

Preload dependency has been linked to microcirculatory impairment, with decreased MFI, PVD, and PORH observed via sublingual videomicroscopy, even when cardiac output remains stable [19,98]. In major abdominal surgery, Bouattour *et al.* demonstrated that vascular filling could correct microcirculatory impairment and recruit vessels in hypovolemic patients [98]. This finding was confirmed during major digestive surgery in which NIRS was used to monitor muscle $StO_2$ and PORH after a vascular occlusion test [19]. Measurements were repeated after anaesthesia induction, before and after each fluid challenge in cases of preload dependency, as assessed by pulse pressure variation or stroke volume variation. The tissue resaturation rates improved by 62% when patients were responsive to fluid challenges in terms of cardiac output (an increase >15%), reflecting coupling between macro- and microcirculation. Notably, tissue resaturation still improved by 26%, even when patients were not responsive in terms of cardiac output, indicating that microcirculatory improvement can occur independently of macrohemodynamic changes. Another study revealed that a 27% decrease in CRT during a passive leg-lift test predicted improvements in tissue perfusion after fluid resuscitation, with a 25% decrease in CRT postvascular filling. This test has a sensitivity of 87% [95% CI, 73–100] and a specificity of 100% [95% CI, 74–100], highlighting its predictive value for assessing fluid responsiveness and improvements in tissue perfusion [99].

In major surgery, both massive vascular filling and inflammation can lead to glycocalyx degradation [85,100,101]. Glycocalyx degradation impairs the endothelial barrier, leading to capillary leakage and tissue oedema, which increases the diffusion distance between capillaries and target cells and contributes to organ failure (Fig. 4) [2,15,102]. However, the links among volume expansion, microcirculatory alterations, increased vascular barrier permeability, and perioperative complications have not been formally established. Notably, the results of a local study of microcirculation may also be influenced by regional variability if they are not compared with systemic indicators.

**Suggestion n°3:** Microcirculatory tools can reveal fluid responsiveness even when macrocirculation shows no fluid responsiveness. Standardised tests should be used to assess fluid responsiveness and microcirculatory response to guide fluid administration, as improvements in microcirculation may occur independently of changes in systemic hemodynamics. Be cautious with massive fluid resuscitation; while fluid challenges can improve microcirculation, excessive volume expansion can lead to glycocalyx degradation and capillary leakage, potentially impairing tissue perfusion.

#### 4.2.4. Uncertainty about transfusion

A systematic review published in 2021 explored the complex relationship between red blood cell (RBC) transfusions and microcirculatory changes in patients with pretransfusion haemoglobin levels between 71 g $L^{-1}$ and 88 g $L^{-1}$ [103]. The patient population significantly influenced the microcirculatory response, with intraoperative, traumatic and hypovolemic haemorrhagic shock patients demonstrating improvements, whereas septic patients generally do not. Preexisting microcirculatory status appeared to be a crucial determinant of transfusion efficacy. Studies on hemodynamically stable patients have produced mixed results, highlighting the complexity of microcirculatory responses.

#### 4.2.5. Monitoring the effect of vasopressors

The effects of vasopressors on intraoperative microcirculation are complex, and few clinical studies have been conducted. Norepinephrine administration to treat intraoperative hypotension does not have adverse effects on sublingual, intestinal or gastric microcirculation during prostatectomy, breast cancer surgery, esophagectomy or cardiac surgery [18,92,104,105]. Dose-dependent, increased free flap skin blood flow has been observed with norepinephrine and dobutamine in 24 patients with

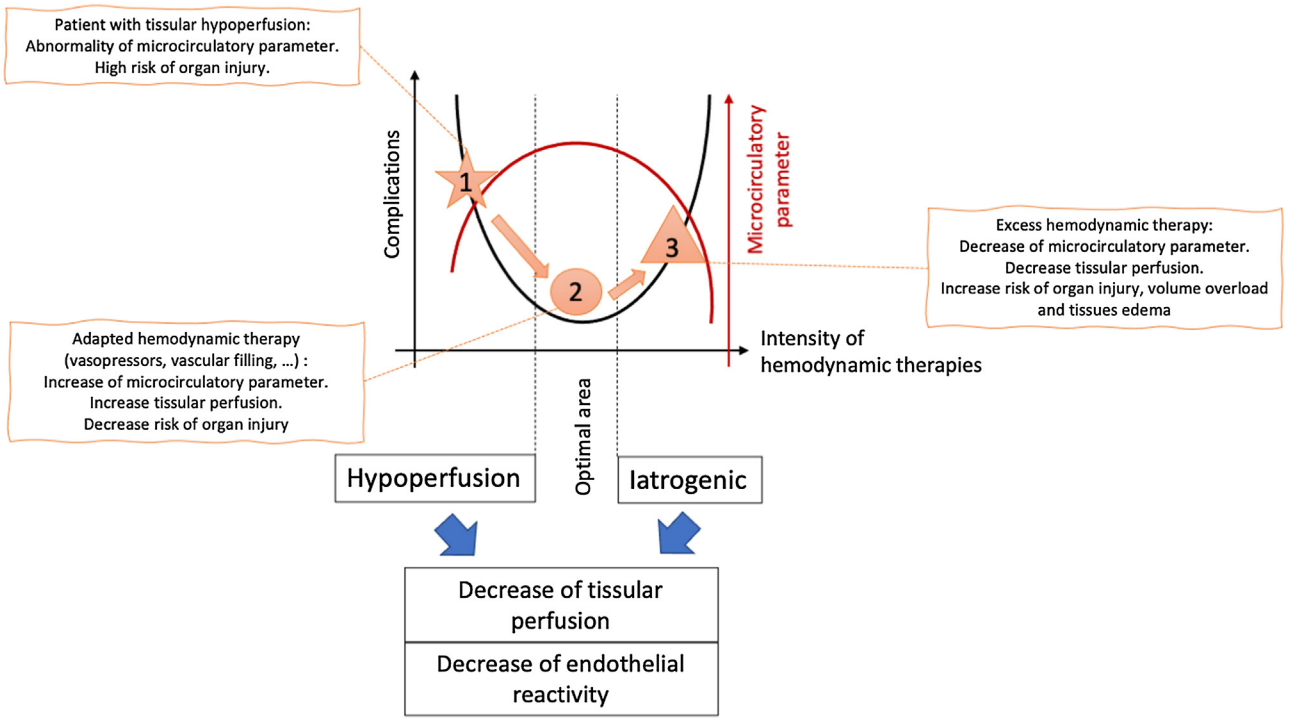



**Fig. 4.** Suggested hemodynamic optimization strategy incorporating a microcirculatory indicator based on two U-shaped curves.
This figure presents a conceptual model based on two U-shaped curves: one representing the frequency of complications and the other a microcirculatory parameter. The aim is to identify the optimal hemodynamic zone where complication risk is minimised and microcirculatory function is optimised. Three different hemodynamic states of a fictional patient are illustrated by the star, circle, and triangle, highlighting how clinical interventions may shift the patient closer to or further from the optimal therapeutic range.

head and neck cancer [106]. The maximal improvement in blood flow occurred with norepinephrine. In contrast, dopexamine and epinephrine infusions decrease blood flow. Vasopressin has been shown to increase endothelin and ischemia of the rectosigmoid mucosa during CPB [107]. Phenylephrine, in the same way, results in compromised tissue perfusion, particularly in sublingual microcirculation [20]. However, if the increase in vasoconstriction is too pronounced, norepinephrine can also impair microcirculatory perfusion, as observed in bone fractures of polytrauma patients and sublingual microcirculation [87,108]. These findings underscore the importance of individualised vasopressor therapy, careful titration, and continuous monitoring of microcirculation to optimise tissue perfusion and minimise potential adverse effects (Fig. 4).

**Suggestion n°4:** Vasopressor therapy generally supports microcirculation, but inappropriate high doses can cause regional vasoconstriction; therefore, vasopressor therapy can be individualised by careful titration, and microcirculatory monitoring should be considered to optimise dosing and minimise adverse effects.

*4.2.6. Specific therapies targeting microcirculation intraoperatively*

Intraoperatively, targeted therapies for patients at risk could also prove beneficial. Several treatments, such as antioxidants, endothelial stabilisers, inodilators, and ischemic preconditioning, have shown promise in improving microcirculatory function in acute conditions such as sepsis, ischemia?reperfusion, and haemorrhagic shock [109–112]. These strategies are promising for future explorations.

*4.3. Suggestions and current limitations for daily clinical use*

These examples highlight the dynamic and sometimes inconsistent nature of hemodynamic coherence, emphasising the potential utility of microcirculation monitoring in guiding volume expansion decisions. For anaesthetists, this task is particularly challenging, as no automated or validated tools currently exist to integrate these indicators into routine clinical practice, and their application remains largely confined to research settings. It is noteworthy that methods for monitoring tissue perfusion differ considerably in cost and complexity. While sublingual videomicroscopy requires substantial investment and training, simpler and more accessible modalities, such as CRT and PI, are already available and can be readily implemented in routine practice. CRT, in particular, offers a simple, safe, and efficient means of assessing tissue perfusion with immediate bedside applicability. The principal limitation in the surgical environment, the restricted access to common assessment sites such as the hands and knees, may be addressed by measuring CRT in alternative locations. As the head is often accessible during surgery, CRT can readily be assessed at the earlobe. Ultimately, the major barrier to routine adoption lies in the limited awareness of both the techniques and the importance of intraoperative tissue perfusion monitoring. Raising awareness and standardising the use of methods already available in operating theatres could represent an important initial step towards broader clinical integration.

Microcirculatory monitoring may offer particular value in specific patient populations and surgical settings. In low-risk surgical patients, a basic level of monitoring using simple tools such as CRT or PI can help identify early signs of tissue hypoperfusion and prompt timely corrective measures. In contrast, an enhanced level of monitoring may be warranted in patients with significant comorbidities (*e.g.* diabetes, chronic renal failure, cardiovascular disease), in operated critically ill patients, or during high-risk surgical procedures where large fluid shifts and blood loss are anticipated. In these contexts, advanced modalities,

including sublingual videomicroscopy or continuous monitoring of urethral PI, could help define an individual's optimal range of arterial pressure and/or cardiac output for tissue perfusion, thereby preventing both hypovolemia and fluid overload. Stratifying monitoring strategies in this way may help optimise resource utilisation while targeting more intensive monitoring to those patients most likely to benefit.

Intraoperative microcirculation assessment could serve two main purposes: guiding volume expansion and monitoring tissue perfusion. A hemodynamic strategy that includes microcirculatory

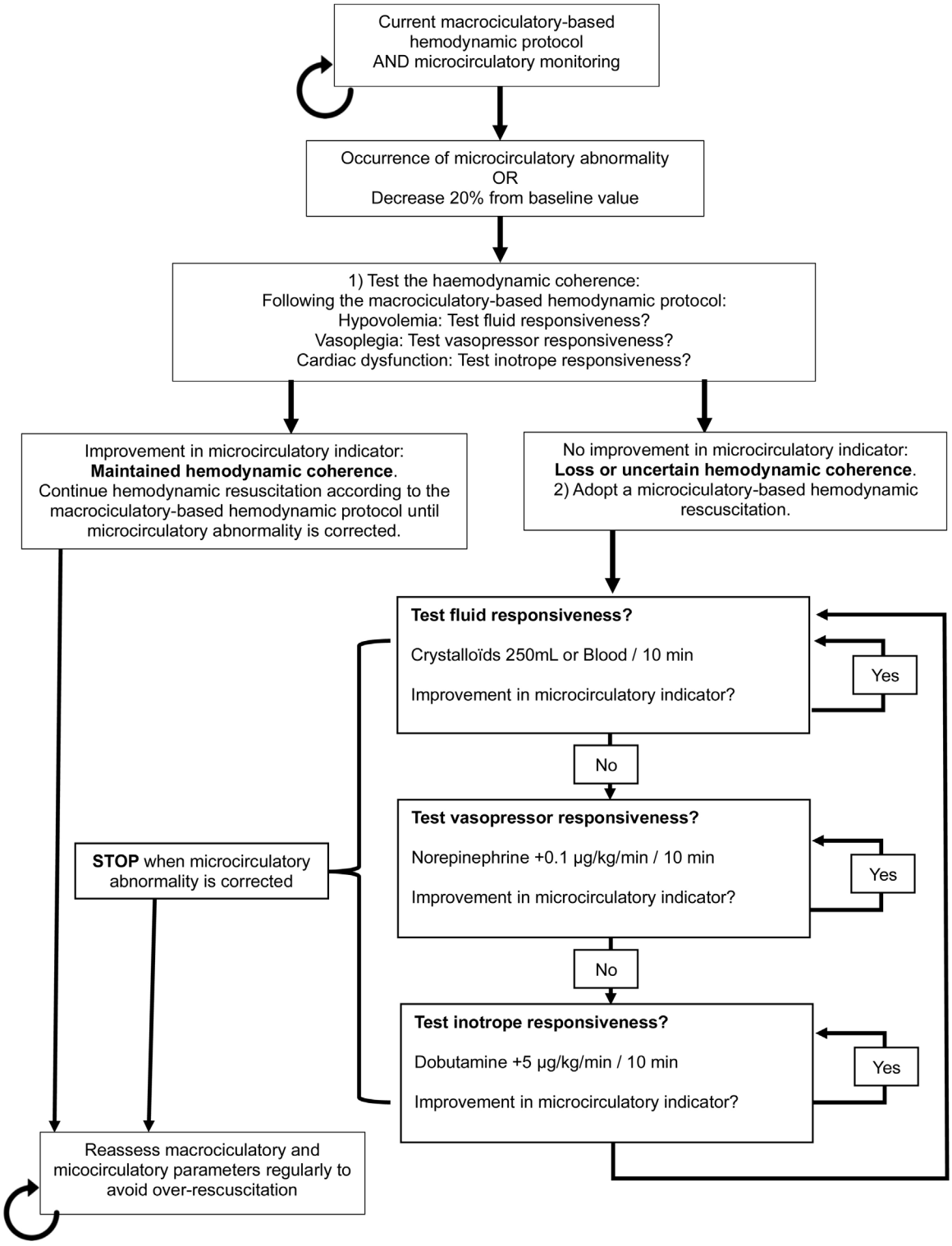

Current macrocirculatory-based hemodynamic protocol AND microcirculatory monitoring
Occurrence of microcirculatory abnormality OR Decrease 20% from baseline value
1) Test the haemodynamic coherence: Following the macrocirculatory-based hemodynamic protocol: Hypovolemia: Test fluid responsiveness? Vasoplegia: Test vasopressor responsiveness? Cardiac dysfunction: Test inotrope responsiveness?
Improvement in microcirculatory indicator: Maintained hemodynamic coherence. Continue hemodynamic resuscitation according to the macrocirculatory-based hemodynamic protocol until microcirculatory abnormality is corrected.
No improvement in microcirculatory indicator: Loss or uncertain hemodynamic coherence. 2) Adopt a microcirculatory-based hemodynamic rescuscitation.
Test fluid responsiveness?
Crystalloïds 250mL or Blood / 10 min
Improvement in microcirculatory indicator?
Yes
No
Test vasopressor responsiveness?
Norepinephrine +0.1 µg/kg/min / 10 min
Improvement in microcirculatory indicator?
Yes
No
Test inotrope responsiveness?
Dobutamine +5 µg/kg/min / 10 min
Improvement in microcirculatory indicator?
Yes
STOP when microcirculatory abnormality is corrected
Reassess macrocirculatory and micocirculatory parameters regularly to avoid over-rescuscitation

**Fig. 5.** Proposed algorithm integrating microcirculation monitoring into intraoperative hemodynamic management.
Different algorithms could be proposed, but key points remain central to their construction: First, microcirculatory monitoring tools, used alongside standard macrocirculatory indicators, facilitate early detection of tissue hypoperfusion intraoperatively. Second, observing improvements in microcirculatory parameters following interventions (such as fluid administration or drug therapy) strongly supports their efficacy, providing guidance on whether interventions should be renewed or discontinued. Finally, while the search for hemodynamic coherence between macro- and microcirculation is not mandatory; the inclusion of microcirculatory assessment helps to validate actions recommended by established macrocirculatory-based management protocol commonly used in clinical practice.

parameters could be based on the double U-curve principle, as depicted in Fig. 4. A simple intraoperative hemodynamic management protocol could involve performing dynamic tests to assess blood volume, pressure and flow adaptation when signs of tissue hypoperfusion arise (Fig. 5). The exact modalities, however, still require further definition. Given the limitations of individual microcirculation and tissue perfusion assessment techniques, a comprehensive evaluation should integrate multiple indicators to mitigate the restricted stand-alone value of most current methods. Moreover, additional studies are needed to validate these approaches and determine their impact on clinical outcomes.

**Suggestion n°5:** Monitor tissue perfusion via a simple method that is already available in addition to macrocirculatory monitoring: A skin perfusion indicator, as CRT appears to be simple, safe and efficient with an immediate reading for clinical practice. A reduction in the CRT after interventions such as fluid resuscitation, vasopressors, or inotropes strongly suggests a beneficial effect of this intervention and supports repeating the intervention as long as an improvement in the indicator is observed.

## 5. Conclusion

A growing body of evidence supports the existence of a continuum between clinical status, microcirculatory function, perioperative outcome, and postoperative organ function. Preoperative microcirculatory assessment has shown potential in predicting complications across diverse surgical settings, suggesting that its integration into standard preoperative evaluation – alongside blood pressure or electrocardiogram – may become routine. The perioperative period, particularly in major surgery or in patients with cardiovascular comorbidities, is a promising field for applying these insights. Preoperative assessment offers a unique opportunity to detect chronic microcirculatory dysfunction in a stable state, before surgical stress exacerbates it. A deeper understanding of microcirculation, its complex interdependence with macrocirculation through hemodynamic coherence and its role in clinical events has the potential to drive the development of personalised medicine in the perioperative period. By identifying individual microcirculatory responses, anaesthesiologists could tailor interventions to better meet the specific needs of each patient, improving outcomes and minimising complications. However, despite its promise, microcirculatory monitoring is not yet ready for routine clinical use. There remains a pressing need for robust studies to identify the most relevant microcirculatory indicators, standardise their interpretation, and integrate them into decision-making frameworks.

## CRediT authorship contribution statement

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

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## Declaration of competing interest

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## Appendix A. Supplementary data

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## References

[1] Büchele GL, Ospina-Tascon GA, De Backer D. How microcirculation data have changed my clinical practice. Curr Opin Crit Care 2007;13:324–31. http://dx.doi.org/10.1097/MCC.0b013e3280c1e5c5.
[2] Ince C, Mayeux PR, Nguyen T, Gomez H, Kellum JA, Ospina-Tascón GA, et al. The endothelium in sepsis. Shock 2016;45:259–70. http://dx.doi.org/10.1097/SHK.0000000000000473.
[3] Brienza N, Biancofiore G, Cavaliere F, Corcione A, De Gasperi A, De Rosa RC, et al. Clinical guidelines for perioperative hemodynamic management of non cardiac surgical adult patients. Minerva Anestesiol 2019;85. http://dx.doi.org/10.23736/S0375-9393.19.13584-5.
[4] Saugel B, Buhre W, Chew MS, Cholley B, Coburn M, Cohen B, et al. Intraoperative haemodynamic monitoring and management of adults having noncardiac surgery: a statement from the European Society of Anaesthesiology and Intensive Care. Eur J Anaesthesiol 2025;42:543–56. http://dx.doi.org/10.1097/EJA.0000000000002174.
[5] Michard F, Biais M, Lobo SM, Futier E. Perioperative hemodynamic management 4.0. Best Pract Res Clin Anaesthesiol 2019;33:247–55. http://dx.doi.org/10.1016/j.bpa.2019.04.002.
[6] Guven G, Hilty MP, Ince C. Microcirculation: physiology, pathophysiology, and clinical application. Blood Purif 2020;49:143–50. http://dx.doi.org/10.1159/000503775.
[7] Yoshimoto M, Yoder MC. Birth of the blood cell. Nature 2009;457:801–3. http://dx.doi.org/10.1038/457801a.
[8] Curry FE, Adamson RH. Endothelial glycocalyx: permeability barrier and mechanosensor. Ann Biomed Eng 2012;40:828–39. http://dx.doi.org/10.1007/s10439-011-0429-8.
[9] Curry FR, Adamson RH. Vascular permeability modulation at the cell, microvessel, or whole organ level: towards closing gaps in our knowledge. Cardiovasc Res 2010;87:218–29. http://dx.doi.org/10.1093/cvr/cvq115.
[10] Hahn RG, Patel V, Dull RO. Human glycocalyx shedding: systematic review and critical appraisal. Acta Anaesthesiol Scand 2021;65:590–606. http://dx.doi.org/10.1111/aas.13797.
[11] Sakr Y, Dubois MJ, De Backer D, Creteur J, Vincent JL. Persistent microcirculatory alterations are associated with organ failure and death in patients with septic shock. Crit Care Med 2004;32:1825–31.
[12] Tachon G, Harrois A, Tanaka S, Kato H, Huet O, Pottecher J, et al. Microcirculatory alterations in traumatic hemorrhagic shock. Crit Care Med 2014;42:1433–41. http://dx.doi.org/10.1097/CCM.0000000000000223.
[13] Ruan Z, Li R, Dong W, Cui Z, Yang H, Ren R. Laser speckle contrast imaging to monitor microcirculation: an effective method to predict outcome in patients with sepsis and septic shock. Front Bioeng Biotechnol 2023;101067739. http://dx.doi.org/10.3389/fbioe.2022.1067739.
[14] Neto AS, Pereira VGM, Manetta JA, Espósito DC, Schultz MJ. Association between static and dynamic thenar near-infrared spectroscopy and mortality in patients with sepsis: a systematic review and meta-analysis. J Trauma Acute Care Surg 2014;76:226–33. http://dx.doi.org/10.1097/TA.0b013e3182a9221f.
[15] Astapenko D, Benes J, Pouska J, Lehmann C, Islam S, Cerny V. Endothelial glycocalyx in acute care surgery – what anaesthesiologists need to know for clinical practice. BMC Anesthesiol 2019;19:238. http://dx.doi.org/10.1186/s12871-019-0896-2.
[16] Ince C. Hemodynamic coherence and the rationale for monitoring the microcirculation. Crit Care 2015;19:S8. http://dx.doi.org/10.1186/cc14726.
[17] De Backer D, Donadello K, Sakr Y, Ospina-Tascon G, Salgado D, Scolletta S, et al. Microcirculatory alterations in patients with severe sepsis: impact of time of assessment and relationship with outcome. Crit Care Med 2013;41:791–9. http://dx.doi.org/10.1097/CCM.0b013e3182742e8b.
[18] Holmgaard F, Vedel AG, Ravn HB, Nilsson JC, Rasmussen LS. Impact of mean arterial pressure on sublingual microcirculation during cardiopulmonary bypass-secondary outcome from a randomized clinical trial. Microcirculation 2018;25e12459. http://dx.doi.org/10.1111/micc.12459.
[19] Futier E, Christophe S, Robin E, Petit A, Pereira B, Desbordes J, et al. Use of near-infrared spectroscopy during a vascular occlusion test to assess the microcirculatory response during fluid challenge. Crit Care 2011;15:R214. http://dx.doi.org/10.1186/cc10449.

[20] Maier S, Hasibeder WR, Hengl C, Pajk W, Schwarz B, Margreiter J, et al. Effects of phenylephrine on the sublingual microcirculation during cardiopulmonary bypass. Br J Anaesth 2009;102:485–91. http://dx.doi.org/10.1093/bja/aep018.
[21] Balogh ZJ, Reumann MK, Gruen RL, Mayer-Kuckuk P, Schuetz MA, Harris IA, et al. Advances and future directions for management of trauma patients with musculoskeletal injuries. Lancet 2012;380:1109–19. http://dx.doi.org/10.1016/S0140-6736(12)60991-X.
[22] Pearse RM, Harrison DA, MacDonald N, Gillies MA, Blunt M, Ackland G, et al. Effect of a perioperative, cardiac Output–Guided hemodynamic therapy algorithm on outcomes following Major gastrointestinal surgery: a randomized clinical trial and systematic review. JAMA 2014;311:2181. http://dx.doi.org/10.1001/jama.2014.5305.
[23] Xu C, Peng J, Liu S, Huang Y, Guo X, Xiao H, et al. Goal-directed fluid therapy versus conventional fluid therapy in colorectal surgery: a meta analysis of randomized controlled trials. Int J Surg 2018;56:264–73. http://dx.doi.org/10.1016/j.ijsu.2018.06.034.
[24] Som A, Maitra S, Bhattacharjee S, Baidya DK. Goal directed fluid therapy decreases postoperative morbidity but not mortality in major non-cardiac surgery: a meta-analysis and trial sequential analysis of randomized controlled trials. J Anesth 2017;31:66–81. http://dx.doi.org/10.1007/s00540-016-2261-7.
[25] Rollins KE, Lobo DN. Intraoperative goal-directed fluid therapy in elective major abdominal surgery: a meta-analysis of randomized controlled trials. Ann Surg 2016;263:465–76. http://dx.doi.org/10.1097/SLA.0000000000001366.
[26] Cardiac output-guided haemodynamic therapy for patients undergoing major gastrointestinal surgery: OPTIMISE II randomised clinical trial. BMJ 2024;387e080439. http://dx.doi.org/10.1136/bmj-2024-080439.
[27] Bakker J, Ince C. Monitoring coherence between the macro and microcirculation in septic shock. Curr Opin Crit Care 2020;26:267–72. http://dx.doi.org/10.1097/MCC.0000000000000729.
[28] Kattan E, Ibarra-Estrada M, Ospina-Tascón G, Hernández G. Perspectives on peripheral perfusion assessment. Curr Opin Crit Care 2023;29:208–14. http://dx.doi.org/10.1097/MCC.0000000000001038.
[29] Brunauer A, Koköfer A, Bataar O, Gradwohl-Matis I, Dankl D, Bakker J, et al. Changes in peripheral perfusion relate to visceral organ perfusion in early septic shock: a pilot study. J Crit Care 2016;35:105–9. http://dx.doi.org/10.1016/j.jcrc.2016.05.007.
[30] van Genderen ME, Paauwe J, de Jonge J, van der Valk RJ, Lima A, Bakker J, et al. Clinical assessment of peripheral perfusion to predict postoperative complications after major abdominal surgery early: a prospective observational study in adults. Crit Care 2014;18:R114. http://dx.doi.org/10.1186/cc13905.
[31] La Via L, Sanfilippo F, Continella C, Triolo T, Messina A, Robba C, et al. Agreement between Capillary Refill Time measured at Finger and Earlobe sites in different positions: a pilot prospective study on healthy volunteers. BMC Anesthesiol 2023;23:30. http://dx.doi.org/10.1186/s12871-022-01920-1.
[32] Hernandez G, Bellomo R, Bakker J. The ten pitfalls of lactate clearance in sepsis. Intensive Care Med 2019;45:82–5. http://dx.doi.org/10.1007/s00134-018-5213-x.
[33] Garcia-Alvarez M, Marik P, Bellomo R. Stress hyperlactataemia: present understanding and controversy. Lancet Diabetes Endocrinol 2014;2:339–47. http://dx.doi.org/10.1016/S2213-8587(13)70154-2.
[34] Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Intensive Care Med 2021;47:1181–247. http://dx.doi.org/10.1007/s00134-021-06506-y.
[35] Palsson-McDermott EM, O'Neill LAJ. The Warburg effect then and now: from cancer to inflammatory diseases. BioEssays 2013;35:965–73. http://dx.doi.org/10.1002/bies.201300084.
[36] Ho KM. Pitfalls in haemodynamic monitoring in the postoperative and critical care setting. Anaesth Intensive Care 2016;44:14–9. http://dx.doi.org/10.1177/0310057X1604400104.
[37] Pope JV, Jones AE, Gaieski DF, Arnold RC, Trzeciak S, Shapiro NI. Multicenter study of Central Venous Oxygen Saturation (ScvO2) as a predictor of mortality in patients with sepsis. Ann Emerg Med 2010;55:40–46.e1. http://dx.doi.org/10.1016/j.annemergmed.2009.08.014.
[38] Textoris J, Fouché L, Wiramus S, Antonini F, Tho S, Martin C, et al. High central venous oxygen saturation in the latter stages of septic shock is associated with increased mortality. Crit Care 2011;15:R176. http://dx.doi.org/10.1186/cc10325.
[39] Bansch P, Flisberg P, Bentzer P. Changes in the sublingual microcirculation during major abdominal surgery and post-operative morbidity: microcirculation and outcome after surgery. Acta Anaesthesiol Scand 2014;58:89–97. http://dx.doi.org/10.1111/aas.12204.
[40] Flick M, Hilty MP, Duranteau J, Saugel B. The microcirculation in perioperative medicine: a narrative review. Br J Anaesth 2024;132:25–34. http://dx.doi.org/10.1016/j.bja.2023.10.033.
[41] On behalf of the Cardiovascular Dynamics Section of the ESICM, Ince C, Boerma EC, Cecconi M, De Backer D, Shapiro NI, et al. Second consensus on the assessment of sublingual microcirculation in critically ill patients: results from a task force of the European Society of Intensive Care Medicine. Intensive Care Med 2018;44:281–99. http://dx.doi.org/10.1007/s00134-018-5070-7.
[42] Koning NJ, Vonk AB, Vink H, Boer C. Side-by-side alterations in glycocalyx thickness and perfused microvascular density during acute microcirculatory alterations in cardiac surgery. Microcirculation 2016;23:69–74. http://dx.doi.org/10.1111/micc.12260.
[43] Miyazaki T, Kuwano H, Kato H, Yoshikawa M, Ojima H, Tsukada K. Predictive value of blood flow in the gastric tube in anastomotic insufficiency after thoracic esophagectomy. World J Surg 2002;26:1319–23. http://dx.doi.org/10.1007/s00268-002-6366-9.
[44] Koning NJ, Simon LE, Asfar P, Baufreton C, Boer C. Systemic microvascular shunting through hyperdynamic capillaries after acute physiological disturbances following cardiopulmonary bypass. Am J Physiol Heart Circ Physiol 2014;307:H967–75. http://dx.doi.org/10.1152/ajpheart.00397.2014.
[45] Uz Z, van Gulik TM, Aydemirli MD, Guerci P, Ince Y, Cuppen D, et al. Identification and quantification of human microcirculatory leukocytes using handheld video microscopes at the bedside. J Appl Physiol (1985) 2018;124:1550–7. http://dx.doi.org/10.1152/japplphysiol.00962.2017.
[46] Uz Z, Ince C, Shen L, Ergin B, van Gulik TM. Real-time observation of microcirculatory leukocytes in patients undergoing major liver resection. Sci Rep 2021;11:4563. http://dx.doi.org/10.1038/s41598-021-83677-0.
[47] Jacquet-Lagrèze M, Magnin M, Allaouchiche B, Abrard S. Is handheld video microscopy really the future of microcirculation monitoring? Crit Care 2023;27:352. http://dx.doi.org/10.1186/s13054-023-04642-z.
[48] Bol ME, Broddin BEK, Delhaas T, Sels JEM, Van De Poll MCG. Variability of microcirculatory measurements in healthy volunteers. Sci Rep 2022;1219887. http://dx.doi.org/10.1038/s41598-022-22947-x.
[49] Hilty MP, Guerci P, Ince Y, Toraman F, Ince C. MicroTools enables automated quantification of capillary density and red blood cell velocity in handheld vital microscopy. Commun Biol 2019;2:217. http://dx.doi.org/10.1038/s42003-019-0473-8.
[50] Coutrot M, Dudoignon E, Joachim J, Gayat E, Vallée F, Dépret F. Perfusion index: physical principles, physiological meanings and clinical implications in anaesthesia and critical care. Anaesth Crit Care Pain Med 2021;40100964. http://dx.doi.org/10.1016/j.accpm.2021.100964.
[51] Agerskov M, Thusholdt ANW, Holm-Sørensen H, Wiberg S, Meyhoff CS, Højlund J, et al. Association of the intraoperative peripheral perfusion index with postoperative morbidity and mortality in acute surgical patients: a retrospective observational multicentre cohort study. Br J Anaesth 2021;127:396–404. http://dx.doi.org/10.1016/j.bja.2021.06.004.
[52] Flick M, Rosenau L, Sadtler H, Kouz K, Krause L, Joosten A, et al. The urethral perfusion index during off-pump coronary artery bypass surgery: an observational study. J Cardiothorac Vasc Anesth 2024;38:417–22. http://dx.doi.org/10.1053/j.jvca.2023.09.015.
[53] Chirnoaga D, Coeckelenbergh S, Ickx B, Van Obbergh L, Lucidi V, Desebbe O, et al. Impact of conventional vs. goal-directed fluid therapy on urethral tissue perfusion in patients undergoing liver surgery: a pilot randomised controlled trial. Eur J Anaesthesiol 2022;39:324–32. http://dx.doi.org/10.1097/EJA.0000000000001615.
[54] Vacheron C-H, Allaouchiche B. Illustration of the loss of haemodynamic coherence during atrial fibrillation using urethral photoplethysmography. BMJ Case Rep 2019;12e230757. http://dx.doi.org/10.1136/bcr-2019-230757.
[55] Akata T, Kanna T, Yoshino J, Higashi M, Fukui K, Takahashi S. Reliability of fingertip skin-surface temperature and its related thermal measures as indices of peripheral perfusion in the clinical setting of the operating theatre. Anaesth Intensive Care 2004;32:519–29. http://dx.doi.org/10.1177/0310057X0403200409.
[56] Weil MH. Tissue PCO2 as universal marker of tissue hypoxia. Minerva Anestesiol 2000;66:343–7.
[57] Vallée F, Nougué H, Mari A, Vodovar N, Dubreuil G, Damoisel C, et al. Variations of cutaneous capnometry and perfusion index during a heating challenge is early impaired in septic shock and related to prognostic in non-septic shock. Shock 2019;51:585–92. http://dx.doi.org/10.1097/SHK.0000000000001216.
[58] Vallée F, Mateo J, Dubreuil G, Poussant T, Tachon G, Ouanounou I, et al. Cutaneous ear lobe P co 2 at 37°C to evaluate microperfusion in patients with septic shock. Chest 2010;138:1062–70. http://dx.doi.org/10.1378/chest.09-2690.
[59] de Wijs CJ, Streng LWJM, Stolker RJ, Ter Horst M, Hoorn EJ, Mahtab EAF, et al. Mitochondrial oxygenation monitoring and acute kidney injury risk in cardiac surgery: a prospective cohort study. J Clin Anesth 2025;101111715. http://dx.doi.org/10.1016/j.jclinane.2024.111715.
[60] Hilderink BN, Crane RF, Arbous SM, van den Bogaard B, Pillay J, Juffermans NP. Low postoperative mitochondrial oxygen tension is an early marker of acute kidney injury after cardiac surgery: a prospective observational study. J Crit Care 2025;88155088. http://dx.doi.org/10.1016/j.jcrc.2025.155088.
[61] Roustit M, Cracowski JL. Assessment of endothelial and neurovascular function in human skin microcirculation. Trends Pharmacol Sci 2013;34:373–84. http://dx.doi.org/10.1016/j.tips.2013.05.007.
[62] Niezen CK, Massari D, Vos JJ, Scheeren TWL. The use of a vascular occlusion test combined with near-infrared spectroscopy in perioperative care: a systematic review. J Clin Monit Comput 2022;36:933–46. http://dx.doi.org/10.1007/s10877-021-00779-w.
[63] Brunt VE, Minson CT. Cutaneous thermal hyperemia: more than skin deep. J Appl Physiol (1985) 2011;111:5–7. http://dx.doi.org/10.1152/japplphysiol.00544.2011.
[64] Greenwood JC, Talebi FM, Jang DH, Spelde AE, Tonna JE, Gutsche JT, et al. Topical nitroglycerin to detect reversible microcirculatory dysfunction in

patients with circulatory shock after cardiovascular surgery: an observational study. Sci Rep 2022;1215257. http://dx.doi.org/10.1038/s41598-022-19741-0.
[65] Hilty MP, Pichler J, Ergin B, Hefti U, Merz TM, Ince C, et al. Assessment of endothelial cell function and physiological microcirculatory reserve by video microscopy using a topical acetylcholine and nitroglycerin challenge. ICMx 2017;5:26. http://dx.doi.org/10.1186/s40635-017-0139-0.
[66] Miranda ACD, Stefani FDCD, Vesco BCD, Carraro Júnior H, Assreuy J, Morello LG, et al. Relationship between peripheral ischemic microvascular reserve, persistent hyperlactatemia, and its temporal dynamics in sepsis: a post hoc study. Crit Care Sci 2023;35. http://dx.doi.org/10.5935/2965-2774.20230348-en.
[67] Feng J, Liu Y, Chu LM, Singh AK, Dobrilovic N, Fingleton JG, et al. Changes in microvascular reactivity after cardiopulmonary bypass in patients with poorly controlled versus controlled diabetes. Circulation 2012;126:S73–80. http://dx.doi.org/10.1161/CIRCULATIONAHA.111.084590.
[68] Jhanji S, Lee C, Watson D, Hinds C, Pearse RM. Microvascular flow and tissue oxygenation after major abdominal surgery: association with post-operative complications. Intensive Care Med 2009;35:671–7. http://dx.doi.org/10.1007/s00134-008-1325-z.
[69] Gokce N, Keaney JF, Hunter LM, Watkins MT, Menzoian JO, Vita JA. Risk stratification for postoperative cardiovascular events via noninvasive assessment of endothelial function: a prospective study. Circulation 2002;105:1567–72. http://dx.doi.org/10.1161/01.cir.0000012543.55874.47.
[70] Gokce N, Keaney JF, Hunter LM, Watkins MT, Nedeljkovic ZS, Menzoian JO, et al. Predictive value of noninvasively determined endothelial dysfunction for long-term cardiovascular events in patients with peripheral vascular disease. J Am Coll Cardiol 2003;41:1769–75. http://dx.doi.org/10.1016/s0735-1097(03)00333-4.
[71] Huang AL, Silver AE, Shvenke E, Schopfer DW, Jahangir E, Titas MA, et al. Predictive value of reactive hyperemia for cardiovascular events in patients with peripheral arterial disease undergoing vascular surgery. Arterioscler Thromb Vasc Biol 2007;27:2113–9. http://dx.doi.org/10.1161/ATVBAHA.107.147322.
[72] McIlroy DR, Chan MTV, Wallace SK, Symons JA, Koo EGY, Chu LCY, et al. Automated preoperative assessment of endothelial dysfunction and risk stratification for perioperative myocardial injury in patients undergoing non-cardiac surgery. Br J Anaesth 2014;112:47–56. http://dx.doi.org/10.1093/bja/aet354.
[73] McIlroy DR, Chan MTV, Wallace SK, Grover A, Koo EGY, Ma J, et al. Is preoperative endothelial dysfunction a potentially modifiable risk factor for renal injury associated with noncardiac surgery? J Cardiothorac Vasc Anesth 2015;29:1220–8. http://dx.doi.org/10.1053/j.jvca.2015.05.116.
[74] Abrard S, Fouquet O, Riou J, Rineau E, Abraham P, Sargentini C, et al. Preoperative endothelial dysfunction in cutaneous microcirculation is associated with postoperative organ injury after cardiac surgery using extracorporeal circulation: a prospective cohort study. Ann Intensive Care 2021;11:4. http://dx.doi.org/10.1186/s13613-020-00789-y.
[75] Abrard S, Streichenberger A, Riou J, Hersant J, Rineau E, Jacquet-Lagrèze M, et al. Preoperative endothelial dysfunction for the prediction of acute kidney injury after cardiac surgery using cardiopulmonary bypass: a pilot study based on a second analysis of the MONS study. Perioper Med 2024;13:12. http://dx.doi.org/10.1186/s13741-024-00364-0.
[76] Abrard S, Lasocki S, Henni S. Pre-operative evaluation of microcirculation for the prediction of complications after cardiac surgery under extracorporeal circulation: study protocol. Eur J Anaesthesiol 2019;36:613. http://dx.doi.org/10.1097/EJA.0000000000000968.
[77] Gillies MA, Sander M, Shaw A, Wijeysundera DN, Myburgh J, Aldecoa C, et al. Current research priorities in perioperative intensive care medicine. Intensive Care Med 2017;43:1173–86. http://dx.doi.org/10.1007/s00134-017-4848-3.
[78] Fromy B, Sigaudo-Roussel D, Gaubert-Dahan ML, Rousseau P, Abraham P, Benzoni D, et al. Aging-associated sensory neuropathy alters pressure-induced vasodilation in humans. J Invest Dermatol 2010;130:849–55. http://dx.doi.org/10.1038/jid.2009.279.
[79] Kruger A, Stewart J, Sahityani R, O'Riordan E, Thompson C, Adler S, et al. Laser Doppler flowmetry detection of endothelial dysfunction in end-stage renal disease patients: correlation with cardiovascular risk. Kidney Int 2006;70:157–64. http://dx.doi.org/10.1038/sj.ki.5001511.
[80] Levy BI, Schiffrin EL, Mourad JJ, Agostini D, Vicaut E, Safar ME, et al. Impaired tissue perfusion: a pathology common to hypertension, obesity, and diabetes mellitus. Circulation 2008;118:968–76. http://dx.doi.org/10.1161/CIRCULATIONAHA.107.763730.
[81] Flick M, Schreiber T-H, Montomoli J, Krause L, de Boer HD, Kouz K, et al. Microcirculatory tissue perfusion during general anaesthesia and noncardiac surgery: an observational study using incident dark field imaging with automated video analysis. Eur J Anaesthesiol 2022;39:582–90. http://dx.doi.org/10.1097/EJA.0000000000001699.
[82] Soares RN, Murias JM, Saccone F, Puga L, Moreno G, Resnik M, et al. Effects of a rehabilitation program on microvascular function of CHD patients assessed by near-infrared spectroscopy. Physiol Rep 2019;7. http://dx.doi.org/10.14814/phy2.14145.
[83] Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345:1368–77. http://dx.doi.org/10.1056/NEJMoa010307.
[84] Jessen MK, Vallentin MF, Holmberg MJ, Bolther M, Hansen FB, Holst JM, et al. Goal-directed haemodynamic therapy during general anaesthesia for non-cardiac surgery: a systematic review and meta-analysis. Br J Anaesth 2022;128:416–33. http://dx.doi.org/10.1016/j.bja.2021.10.046.
[85] Chappell D, Bruegger D, Potzel J, Jacob M, Brettner F, Vogeser M, et al. Hypervolemia increases release of atrial natriuretic peptide and shedding of the endothelial glycocalyx. Crit Care 2014;18:538. http://dx.doi.org/10.1186/s13054-014-0538-5.
[86] Kelm DJ, Perrin JT, Cartin-Ceba R, Gajic O, Schenck L, Kennedy CC. Fluid overload in patients with severe sepsis and septic shock treated with early goal-directed therapy Is associated with increased acute need for fluid-related medical interventions and Hospital death. Shock 2015;43:68–73. http://dx.doi.org/10.1097/SHK.0000000000000268.
[87] Dubin A, Pozo MO, Casabella CA, Pálizas F, Murias G, Moseinco MC, et al. Increasing arterial blood pressure with norepinephrine does not improve microcirculatory blood flow: a prospective study. Crit Care 2009;13:R92. http://dx.doi.org/10.1186/cc7922.
[88] De Backer D, Creteur J, Preiser JC, Dubois MJ, Vincent JL. Microvascular blood flow is altered in patients with sepsis. Am J Respir Crit Care Med 2002;166:98–104.
[89] Flick M, Jannsen GP, Krause L, Montomoli J, Pollok F, Moll-Khosrawi P, et al. The effect of major abdominal surgery on the sublingual microcirculation: an observational study. Can J Anesth/J Can Anesth 2025;72:768–79. http://dx.doi.org/10.1007/s12630-025-02941-3.
[90] Flick M, Briesenick-Weskamm L, Sierzputowski P, Süykers M-C, Moll-Khosrawi P, Krause L, et al. The effects of maximizing stroke volume versus maintaining preoperative resting cardiac index on oxygen delivery, oxygen consumption, and microcirculatory tissue perfusion in patients having major abdominal surgery: the exploratory randomized CUSTOM trial. J Clin Anesth 2025;106111905. http://dx.doi.org/10.1016/j.jclinane.2025.111905.
[91] Coeckelenbergh S, Entzeroth M, Van Der Linden P, Flick M, Soucy-Proulx M, Alexander B, et al. Assisted fluid management and sublingual microvascular flow during High-risk abdominal surgery: a randomized controlled trial. Anesth Analg 2025;140:1149–58. http://dx.doi.org/10.1213/ANE.0000000000007097.
[92] Flick M, Briesenick L, Peine S, Scheeren TWL, Duranteau J, Saugel B. The effect of moderate intraoperative blood loss and norepinephrine therapy on sublingual microcirculatory perfusion in patients having open radical prostatectomy: an observational study. Eur J Anaesthesiol 2021;38:459–67. http://dx.doi.org/10.1097/EJA.0000000000001434.
[93] Kim TK, Cho YJ, Min JJ, Murkin JM, Bahk JH, Hong DM, et al. Microvascular reactivity and clinical outcomes in cardiac surgery. Crit Care 2015;19:316. http://dx.doi.org/10.1186/s13054-015-1025-3.
[94] Salgado MA, Salgado-Filho MF, Reis-Brito JO, Lessa MA, Tibirica E. Effectiveness of laser Doppler perfusion monitoring in the assessment of microvascular function in patients undergoing on-pump coronary artery bypass grafting. J Cardiothorac Vasc Anesth 2014;28:1211–6. http://dx.doi.org/10.1053/j.jvca.2014.03.003.
[95] Hernández G, Ospina-Tascón GA, Damiani LP, Estenssoro E, Dubin A, Hurtado J, et al. Effect of a resuscitation strategy targeting peripheral perfusion Status vs serum lactate levels on 28-day mortality among patients with septic shock: the ANDROMEDA-shock randomized clinical trial. JAMA 2019;321:654. http://dx.doi.org/10.1001/jama.2019.0071.
[96] Zampieri FG, Damiani LP, Bakker J, Ospina-Tascón GA, Castro R, Cavalcanti AB, et al. Effects of a resuscitation strategy targeting peripheral perfusion Status versus serum lactate levels among patients with septic shock. A Bayesian reanalysis of the ANDROMEDA-shock trial. Am J Respir Crit Care Med 2020;201:423–9. http://dx.doi.org/10.1164/rccm.201905-0968OC.
[97] Trzeciak S, McCoy JV, Phillip Dellinger R, Arnold RC, Rizzuto M, Abate NL, et al. Early increases in microcirculatory perfusion during protocol-directed resuscitation are associated with reduced multi-organ failure at 24 h in patients with sepsis. Intensive Care Med 2008;34:2210–7. http://dx.doi.org/10.1007/s00134-008-1193-6.
[98] Bouattour K, Teboul J-L, Varin L, Vicaut E, Duranteau J. Preload dependence Is associated with reduced sublingual microcirculation during Major abdominal surgery. Anesthesiology 2019;130:541–9. http://dx.doi.org/10.1097/ALN.0000000000002631.
[99] Jacquet-Lagrèze M, Bouhamri N, Portran P, Schweizer R, Baudin F, Lilot M, et al. Capillary refill time variation induced by passive leg raising predicts capillary refill time response to volume expansion. Crit Care 2019;23:281. http://dx.doi.org/10.1186/s13054-019-2560-0.
[100] Wiesinger A, Peters W, Chappell D, Kentrup D, Reuter S, Pavenstädt H, et al. Nanomechanics of the endothelial glycocalyx in experimental sepsis. PLoS One 2013;8e80905. http://dx.doi.org/10.1371/journal.pone.0080905.
[101] Rorije NMG, Olde Engberink RHG, Chahid Y, Van Vlies N, Van Straalen JP, Van Den Born B-JH, et al. Microvascular permeability after an acute and chronic Salt load in healthy subjects. Anesthesiology 2018;128:352–60. http://dx.doi.org/10.1097/ALN.0000000000001989.
[102] Rubio-Gayosso I, Platts SH, Duling BR. Reactive oxygen species mediate modification of glycocalyx during ischemia-reperfusion injury. Am J Physiol Heart Circ Physiol 2006;290:H2247–56. http://dx.doi.org/10.1152/ajpheart.00796.2005.
[103] Liu W, He H, Ince C, Long Y. The effect of blood transfusion on sublingual microcirculation in critically ill patients: a scoping review. Microcirculation 2021;28e12666. http://dx.doi.org/10.1111/micc.12666.

[104] Chiarandini P, Pompei L, Costa MG, Vetrugno L, Ronga F, Contin R, et al. Effects of catecholamines on microcirculation during General inhalation anesthesia. J Cardiothorac Vasc Anesth 2013;27:1239–45. http://dx.doi.org/10.1053/j.jvca.2013.03.036.

[105] Ambrus R, Achiam MP, Secher NH, Svendsen MBS, Rünitz K, Siemsen M, et al. Evaluation of gastric microcirculation by laser speckle contrast imaging during esophagectomy. J Am Coll Surg 2017;225:395–402. http://dx.doi.org/10.1016/j.jamcollsurg.2017.06.003.

[106] Eley KA, Young JD, Watt-Smith SR. Epinephrine, norepinephrine, dobutamine, and dopexamine effects on Free flap skin blood flow. Plast Reconstr Surg 2012;130:564–70. http://dx.doi.org/10.1097/PRS.0b013e31825dbf73.

[107] Bomberg H, Bierbach B, Flache S, Scheuer C, Novák M, Schäfers H-J, et al. Vasopressin induces rectosigmoidal mucosal ischemia during cardiopulmonary bypass: VASOPRESSIN induces rectosigmoidal mucosal ischemia. J Card Surg 2014;29:108–15. http://dx.doi.org/10.1111/jocs.12242.

[108] Koch L, Orth M, Fink T, Meiser A, Volk T, Menger MD, et al. Lower oxygen saturation with higher rates of norepinephrine in bone fractures of polytrauma patients: a pilot study. Crit Care 2023;27:367. http://dx.doi.org/10.1186/s13054-023-04657-6.

[109] Lavillegrand J-R, Raia L, Urbina T, Hariri G, Gabarre P, Bonny V, et al. Vitamin C improves microvascular reactivity and peripheral tissue perfusion in septic shock patients. Crit Care 2022;26:25. http://dx.doi.org/10.1186/s13054-022-03891-8.

[110] Lopez E, Peng Z, Kozar RA, Cao Y, Ko TC, Wade CE, et al. Antithrombin III contributes to the protective effects of fresh frozen plasma following hemorrhagic shock by preventing syndecan-1 shedding and endothelial barrier disruption. Shock 2020;53:156–63. http://dx.doi.org/10.1097/SHK.0000000000001432.

[111] Aggarwal S, Randhawa PK, Singh N, Jaggi AS. Preconditioning at a distance: involvement of endothelial vasoactive substances in cardioprotection against ischemia-reperfusion injury. Life Sci 2016;151:250–8. http://dx.doi.org/10.1016/j.lfs.2016.03.021.

[112] Bar S, Diaper J, Fontao F, Belin X, Abrard S, Albu G, et al. Early and concomitant administration of norepinephrine and ilomedin improves microcirculatory perfusion without impairing macrocirculation in an intestinal ischemia-reperfusion injury swine model: a randomized experimental trial. Shock 2025;63:606–13. http://dx.doi.org/10.1097/SHK.0000000000002533.